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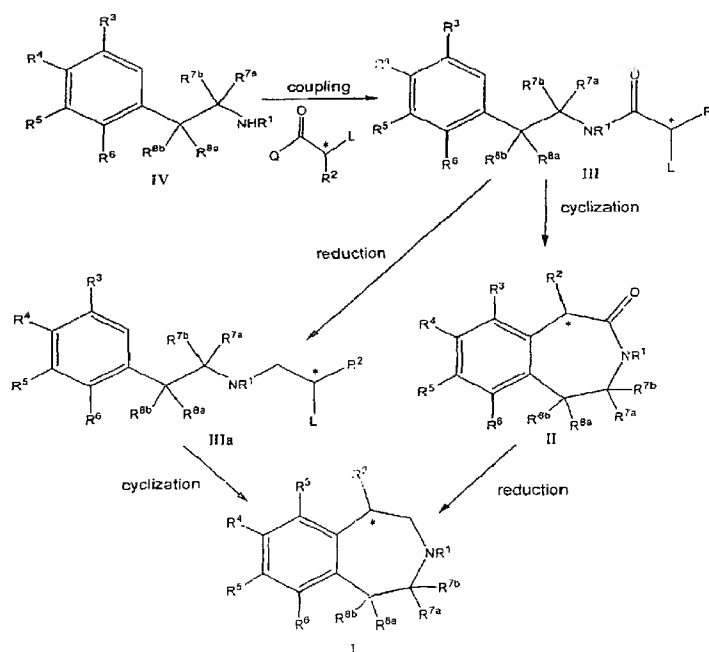
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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[Continued on next page]

(54) Title: BENZAZEPINE DERIVATIVES USEFUL FOR THE TREATMENT OF 5HT_{2C} RECEPTOR ASSOCIATED DISEASES



(57) Abstract: The present invention provides processes and intermediates for the preparation of 3-benzazepines and salts thereof which can be useful as serotonin (5-HT) receptor agonists for the treatment of, for example, central nervous system disorders such as obesity.



ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/019279

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D223/16 A61K31/55 A61P25/00 C07C233/13

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CH 500 194 A (CIBA-GEIGY AG) 15 December 1970 (1970-12-15) abstract claims table, last example column 7 - column 8	28
Y	ORITO ET AL: "TOTAL SYNTHESIS OF PROTOPINE ALKALOIDS" HETEROCYCLES, vol. 14, no. 1, 1980, pages 11-13, XP001205081 SCHEME page 12	28

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

14 March 2005

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24.05.05

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/019279

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 03/086306 A2 (ARENA PHARMACEUTICALS, INC., USA) 23 October 2003 (2003-10-23) abstract examples claims	28
Y	----- CHANG, WEI K. ET AL: "Dopamine receptor binding properties of some 2,3,4,5-tetrahydro-1H-3- benzazepin-7-ols with nonaromatic substituents in the 5-position" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 2(5), 399-402 CODEN: BMCLE8; ISSN: 0960-894X, 1992, XP002306864 abstract Scheme 1 page 400 page 401; table 1	1
X	page 400; example 4	314
Y	----- LADD D L ET AL: "SYNTHESIS AND DOPAMINERGIC BINDING OF 2-ARYLDOPAMINE ANALOGUES: PHENETHYLAMINES, 3-BENZAZEPINES, AND 9-(AMINOMETHYL)FLUORENES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 29, no. 10, October 1986 (1986-10), pages 1904-1912, XP002031848 ISSN: 0022-2623 schemes III,IV page 1907	1
X	page 1907; example 26b	314
X	----- EP 0 285 919 A1 (SCHERING CORP., USA) 12 October 1988 (1988-10-12) abstract examples; tables claims Schemes page 8 - page 9 Schemes page 12	1-138
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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/019279

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PAUVERT M ET AL: "Silver nitrate-promoted ring enlargement of 1-tribromomethyl-1,2-dihydro- and 1-tribromomethyl-1,2,3,4-tetrahydro-isoquinoline derivatives: application to the synthesis of the anti-anginal zatebradine" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 44, no. 22, 26 May 2003 (2003-05-26), pages 4203-4206, XP004423070 ISSN: 0040-4039 page 4205; example 16</p> <p>-----</p>	314
X	<p>DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ORITO, KAZUHIKO ET AL: "Synthetic studies of heterocyclic compounds. I. Alkylation and acylation of 1,2,4,5-tetrahydro-3-methyl-3H-3-benzazepin-2-one" XP002321044 retrieved from STN Database accession no. 1980:407990 abstract & HOKKAIDO DAIGAKU KOGAKUBU KENKYU HOKOKU, (96), 41-4 CODEN: HDKKAA; ISSN: 0385-602X, 1979,</p> <p>-----</p>	314
X	<p>ORITO KAZUHIKO ET AL: "Benzolactams. I. Alkylation of 1,2,4,5-tetrahydro-3-methyl-3H-3-benzazepin-2-one with sodium hydride and alkyl halide" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 36, no. 8, 1980, pages 1017-1021, XP002171212 ISSN: 0040-4020 page 1017; figure 2 page 1019; table 4</p> <p>-----</p>	314
X	<p>DE 19 44 121 A1 (LABORATOIRE HOUDE) 19 March 1970 (1970-03-19) claim 3; figure D examples</p> <p>-----</p>	314
X	<p>FUCHS ET AL: "TOTAL SYNTHESIS OF (+)-LENNOXAMINE AND (+)-APHANORPHINE BY INTRAMOLECULAR ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS OF 2-AMIDOACROLEINS" ORG. LETT., vol. 3, no. 24, 2001, pages 3923-3925, XP002321043 page 3925; compound 22</p> <p>-----</p>	314

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/019279

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-138, 314-340 (part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-138,314 -340(part)

Preparation of compounds according to formula (I) via intermediates according to formula (II)

2. claims: 139-289,314 -340(part)

Preparation of compounds according to formula (I) via intermediates according to formula (IIIa)

3. claims: 290-313,341-347

Method of resolving a mixture of compounds according to formulae (Ia) and (Ib), Compounds according to formulae (Ia) and (Ib) useful as serotonin (5-HT) receptor agonists for the treatment of CNS related diseases

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/019279

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
CH 500194	A	15-12-1970	NONE	
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